AMBIENT ENVIRONMENT

Humidity and immunity

Proc. Natl Acad. Sci. USA https://doi.org/10.1073/pnas.1902840116 (2019)

Infection with respiratory viruses often increases during the colder and less-humid winter months; however, the host-intrinsic factors that contribute to this enhanced susceptibility have remained largely unclear. Iwasaki and colleagues, in the *Proceedings of the National Academy of Sciences*, report on infection with influenza A virus in mice kept under normal or low ambient humidity. Infection under low-humidity conditions results in worse symptoms, less-efficient epithelial repair, impaired mucociliary and innate immune cell–dependent clearance of the virus and reduced control of viral spreading. Furthermore, the expression of key interferon-regulated genes is also reduced under low relative humidity. The mechanism that underpins these diverse impairments seen under low humidity remains unknown but might be related to the induction of stress responses. *ZF*

https://doi.org/10.1038/s41590-019-0434-x

TUMOR IMMUNOTHERAPY

Targeting T_{reg} cells

Nature https://doi.org/10.1038/s41586-019-1215-2 (2019)

The immunosuppressive function of regulatory T cells (T_{reg} cells) counteracts the effectiveness of tumor immunotherapy. In *Nature*, Mempel and colleagues show that disruption of the CARMA1–BCL10–MALT1 signalosome complex in T_{reg} cells leads to production of the cytokine IFN-γ in these cells and the initiation of tumor control. Homozygous deletion of *Carma1* in T_{reg} cells (via *Foxp3*-Cre) in mice results in T_{reg} cell secretion of IFN-γ and multi-organ inflammation, but heterozygous deletion does not, whereas both homozygous tumor-infiltrating CARMA1-deficient T_{reg} cells and their heterozygous counterparts secrete IFN-γ and are sufficient to diminish tumor growth. Acute deletion of CARMA1 in T_{reg} cells reduces growth in already established tumors, and both constitutive deletion and acute deletion of CARMA1 in T_{reg} cells trigger expression of the inhibitory ligand PD-L1 on tumor cells. Inhibitors of the paracaspase activity of MALT1 have effects similar to those of the T_{reg} cell deletion of CARMA1 and act in synergy with treatment with antibody to the inhibitory receptor PD-1 to induce tumor control and relapse-free rejection in checkpoint blockade–resistant tumors. *IV*

https://doi.org/10.1038/s41590-019-0435-9

EBOLA INFECTION

Protective Ig responses

Cell https://doi.org/10.1016/j.cell.2019.04.036 (2019)

Recent outbreaks of Ebola virus (EV) have prompted the need to identify correlates of humoral protection. In *Cell*, Davis et al. report the findings of a longitudinal study of human antibody responses in patients who survived infection with EV. Despite a robust B cell response to viral proteins early after infection, neutralizing anti-viral responses arose months after infection. Similarly, somatic hypermutation frequencies and immunoglobulin G4 responses arose much later. Analysis of protective neutralizing monoclonal antibodies (mAbs) reveals common EV glycoprotein core elements that might be targeted by vaccines. Multiple independent clones use IGHV3-13*03 variable segments and express a complementarity-determining region 3 of 12 amino acids that includes central phenylalanine–glycine residues. Notably, in vitro screening assays with EV glycoprotein successfully discriminate neutralizing mAbs from non-neutralizing mAbs, which might prove useful in vaccine-development studies. *LAD*

https://doi.org/10.1038/s41590-019-0437-7

MUCOSAL IMMUNOLOGY

Food tolerance

J. Clin. Invest. **129**, 1972–1983 (2019)

The gut is continually exposed to dietary antigens, but how tolerance is maintained in the face of this potential stimulus is still not entirely clear. In the *Journal of Clinical Investigation*, Steinhoff and colleagues look at the fate of T cells in the Peyer's patches of normal mice. A conventional diet results in the microbiome-independent accumulation of distinctive Helios$^+$Foxp3$^-$ CD4$^+$ T cells that are non-suppressive and have apoptotic and exhausted signatures. Generation of Helios$^+$Foxp3$^-$ CD4$^+$ T cells in the Peyer's patches requires stimulation via the T cell antigen receptor, and mice fed an elemental, antigen-free diet have fewer of these cells. Efferocytosis of Helios$^+$Foxp3$^-$ CD4$^+$ T cells by macrophages results in their production of the cytokine IL-10. These findings suggest that food antigens trigger T cell death in the small intestine, which enforces a tolerogenic response. *ZF*

https://doi.org/10.1038/s41590-019-0431-0

ADIPOSE-TISSUE HOMEOSTASIS

Fat IL-33 sources

Sci. Immunol. **4**, eaaw3658 & eaax0416 (2019)

IL-33 is a unique nuclear cytokine that serves 'alarmin' roles after it is released from cells; however, IL-33 also has homeostatic roles in various tissues, including adipose tissues. In *Science Immunology*, Spallanzani et al. and Mallakõiv et al. identify the adipose tissue–resident cells that produce IL-33 at steady state to maintain tissue homeostasis. Lin$^-$Sca-1$^+$ mesenchymal cells that express podoplanin and the growth-factor receptor PDGFRα are the main source of IL-33 in adipose tissues. Spallanzani et al. show that a regulatory feedback axis exists between IL-33$^+$ stromal cells and adipose-resident regulatory T cells that express the IL-33 receptor ST2. Mallakõiv et al. show that PDGFRα$^+$ IL-33$^+$ mesenchymal cells likewise interact with ST2$^+$ group 2 innate lymphoid cells to promote their expression of IL-5 and recruitment of eosinophils to adipose tissues. Obesity alters this homeostatic cellular network and promotes inflammatory responses. *LAD*

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